

Appendix I: Pooled PROTECT AF and PREVAIL Subgroup Analyses

There were no statistically significant treatment by subgroup interactions in the pooled PROTECT AF and PREVAIL analysis for the efficacy endpoint, the mechanism of action endpoint, and the endpoint of ischemic stroke (all interaction p-values > 0.40).

For the efficacy endpoint, hazard ratios for all subgroups were less than 1, indicating favorable results for the device group while for both the mechanism of action endpoint and ischemic stroke, hazard ratios for all subgroups were above 1, indicating favorable results for the control group. However, for all three of the endpoints, none of the subgroup specific results yielded statistically significant differences between the treatment and control group. The upper bounds of the confidence intervals for the efficacy endpoint was generally consistent with non-inferiority with most values less than 1.75 or 2.0. The upper bounds of the confidence intervals for the other endpoints were generally not consistent with non-inferiority.

Table 1: Pooled PROTECT AF and PREVAIL – Efficacy Endpoint

Subgroup	Level	N (WATCHMAN)	N (Control)	Hazard Ratio	95% Lower Confidence Limit for Hazard Ratio	95% Upper Confidence Limit for Hazard Ratio	Subgroup Chi-sq P- value	Interaction Chi-sq P- value
Age >= 75	No	402	190	0.802	0.423	1.522	0.5000	0.9008
Age >= 75	Yes	330	192	0.819	0.503	1.335	0.4241	.
CHF	No	545	284	0.715	0.438	1.165	0.1776	0.5509
CHF	Yes	187	98	0.931	0.493	1.758	0.8245	.
Diabetes	No	528	269	0.691	0.425	1.124	0.1364	0.4059
Diabetes	Yes	204	113	0.984	0.519	1.866	0.9598	.
History of TIA/Stroke	No	570	292	0.865	0.527	1.421	0.5671	0.6074
History of TIA/Stroke	Yes	162	90	0.703	0.377	1.310	0.2671	.
Hypertension	No	79	28	0.760	0.264	2.188	0.6113	0.8664
Hypertension	Yes	653	354	0.754	0.496	1.146	0.1864	.

Table 2: Pooled PROTECT AF and PREVAIL – Mechanism of Action Endpoint

Subgroup	Level	N (WATCHMAN)	N (Control)	Hazard Ratio	95% Lower Confidence Limit for Hazard Ratio	95% Upper Confidence Limit for Hazard Ratio	Subgroup Chi-sq P- value	Interaction Chi-sq P- value
Age >= 75	No	402	190	1.919	0.541	6.803	0.3127	0.7708
Age >= 75	Yes	330	192	1.538	0.677	3.492	0.3039	.
CHF	No	545	284	1.299	0.539	3.134	0.5602	0.5562
CHF	Yes	187	98	2.026	0.672	6.106	0.2098	.
Diabetes	No	528	269	1.408	0.626	3.164	0.4081	0.6666
Diabetes	Yes	204	113	1.982	0.546	7.203	0.2986	.
History of TIA/Stroke	No	570	292	1.696	0.621	4.633	0.3025	0.8784
History of TIA/Stroke	Yes	162	90	1.506	0.589	3.849	0.3926	.
Hypertension	No	79	28	1.183	0.246	5.697	0.8339	0.7875
Hypertension	Yes	653	354	1.545	0.721	3.311	0.2634	.

Table 3: Pooled PROTECT AF and PREVAIL – Ischemic Stroke

Subgroup	Level	N (WATCHMAN)	N (Control)	Hazard Ratio	95% Lower Confidence Limit for Hazard Ratio	95% Upper Confidence Limit for Hazard Ratio	Subgroup Chi-sq P- value	Interaction Chi-sq P- value
Age >= 75	No	402	190	2.568	0.748	8.815	0.1339	0.5293
Age >= 75	Yes	330	192	1.607	0.712	3.628	0.2539	.
CHF	No	545	284	1.758	0.754	4.097	0.1915	0.9388
CHF	Yes	187	98	1.892	0.623	5.750	0.2609	.
Diabetes	No	528	269	1.600	0.721	3.549	0.2475	0.6120
Diabetes	Yes	204	113	2.371	0.669	8.402	0.1812	.
History of TIA/Stroke	No	570	292	1.900	0.705	5.119	0.2044	0.9502
History of TIA/Stroke	Yes	162	90	1.804	0.720	4.518	0.2078	.
Hypertension	No	79	28	1.183	0.246	5.697	0.8339	0.6369
Hypertension	Yes	653	354	1.854	0.880	3.906	0.1045	.